[Reprinted from The Philadelphia Monthly Medical Journal, July 1, 1899.

EPIDEMIC CEREBROSPINAL MENINGITIS: REPORT OF THIRTY-FOUR CASES, WITH ESPECIAL REFERENCE TO THE BACTERIOLOGIC FEATURES OF THE DISEASE.*

By R. B. H. GRADWOHL, M.D.,
of St. Louis, Mo.
Bacteriologist to the St. Louis City Hospital, etc.

The attention of the medical world has been frequently called to epidemic cerebrospinal meningitis during the past few decades, and, by means of the almost perfect methods of bacteriologic research now in vogue, very satisfactory results have been obtained in ascertaining the true character of the disease in its recent visitations with us. We find in recent years that several rather extensive epidemics have been reported by competent bacteriologists, viz., that of Barker and Flexner of an outbreak at Lonaconing, Maryland, in 1893;[1] that of Jaeger, of an outbreak in the garrison at Stuttgart in 1895;[2] that of Councilman, Mallory and Wright, of an epidemic which raged in Boston through the winter and spring of 1897;[3] and lastly that of Class, who has very recently described an epidemic in Chicago during the year 1898.[4] It has been my good fortune to have seen 34 cases of this disease during the past winter and spring, as part of the epidemic which has been raging in St. Louis. All of these cases were seen by me in the wards of the St. Louis City Hospital, where I had the opportunity of studying the disease from a clinical, bacteriologic, and pathologic standpoint. My bacteriologic and pathologic work was carried on in the laboratory of bacteriology,

*From the Laboratory of Bacteriology of the Medical Department of Washington University.

medical department of Washington University. I wish to express my indebtedness to Dr. Amand Ravold, professor of bacteriology in the medical department of Washington University, for many favors extended to me while doing this work.

In looking over the literature upon this subject, I have been greatly impressed by the superiority of the reports of the epidemics just quoted over the reports of earlier epidemics at home and abroad, beginning with the first definite description of an epidemic of cerebrospinal meningitis by Vieussieu, in Geneva, in 1805.[5] We are not justified in accepting the reports of probable epidemics of this disease which occurred before the beginning of this century, as the accounts are meager, unsatisfactory and indefinite, so far as a positive establishment of the disease-outbreak is concerned. Hirsch divides the outbreaks of the disease into 4 periods: the first, from 1805 to 1830, in which the disease prevailed principally in the United States; the second, from 1837 to 1850, when it prevailed principally in France and extended from France into Algiers, being carried by the French troops on their Algerian campaign; the third, from 1855 to 1875, when it prevailed principally in Germany; and the fourth, from 1875 to the present time, in which the disease has appeared in small epidemics in a number of places, both in Europe and in this country.

It seems strange that the first definite description of the microorganism which is now justly held to be the specific cause of epidemic cerebrospinal meningitis was considered by Weichselbaum, its discoverer, to be the cause of sporadic cerebrospinal meningitis.[6] Weichselbaum, in 1887, reported 6 cases of cerebrospinal meningitis in which he discovered a microorganism which he called the diplococcus intracellularis, because it was found within the pus-cells of the cerebrospinal fluid. He did not, however, see its relationship to the disease as it exists in epidemic form. It was not until the report of Jaeger's 12 cases in the garrison at Stuttgart[7] that attention was called to the diplococcus intracellularis as the probable specific microorganism of epidemic cerebrospinal

meningitis. Since that time, in all the epidemics which have been reported, that microorganism has been almost constantly present.

There has been some dispute as to the identity or the nonidentity of the diplococcus intracellularis and the diplococcus pneumoniae. Barker and Flexner say[8] that in the epidemic which they studied at Lo-

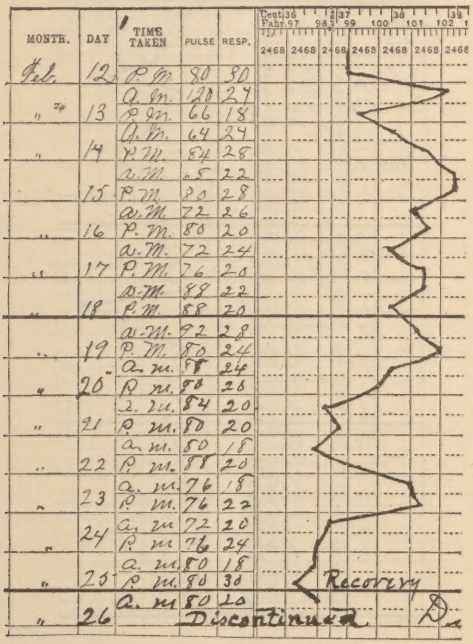

FIG. 1.

naconing they discovered a microorganism which, while behaving much like the micrococcus lanceolatus, might have been a variety of the diplococcus intracellularis meningitidis. In other words, they assume that there is probably some relationship between the diplococcus intracellularis and the micrococcus lanceolatus, not only morphologic but also biologic. On the other hand, we must take into consideration

the disparity between these two microorganisms in their morphologic, cultural and pathogenic characteristics. Councilman, in the Boston epidemic of 1898, found the diplococcus intracellularis in 111 cases, and thus proved its constant presence, adding another confirmation to the statement of Jaeger that this is the essential etiologic factor in the production of

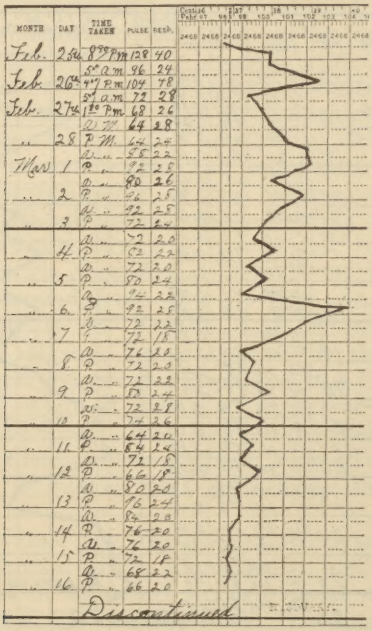

FIG. 2.

pidemic cerebrospinal meningitis. More recently, Class has studied an epidemic of 38 cases in Chicago.[9] It is unfortunate from a statistical point of view that he was only able to perform lumbar puncture in 5 of the 38 cases; nevertheless, he found the diplococcus intracellularis in these 5 cases and would undoubtedly have found it in the other cases had not adverse circumstances forbidden the performance of

lumbar puncture. In the 34 cases which I have seen the diplococcus intracellularis was demonstrated both in fluid obtained by lumbar puncture and from the meninges postmortem, in 33 instances; the micrococcus lanceolatus was found in the other case. This case in which the micrococcus lanceolatus was found was in its clinical behavior identical with the cases pro-

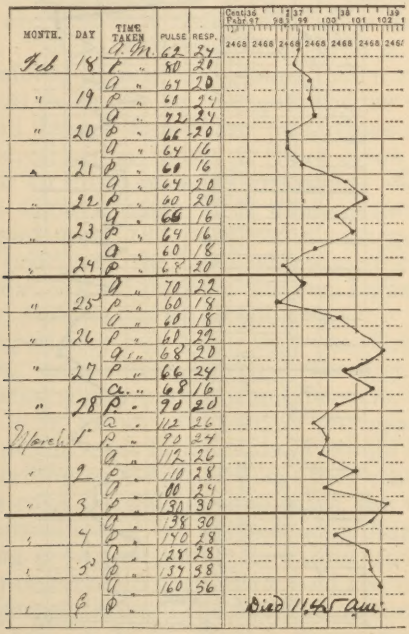

FIG. 3.

duced by the diplococcus intracellularis. No other explanation for its presence can be found than that it was a sporadic case which had become entangled in the whirl of the epidemic cases. Confronted with the bacteriologic findings in these several epidemics, we are warranted in accepting the diplococcus intracellularis as the specific microorganic exciting agent in the production of epidemic cerebrospinal meningitis.

In my investigation of this microorganism, I have followed the plan laid down by the Committee of American Bacteriologists in their report to the Committee on the Pollution of Water-Supplies of the American Public-Health Association.[10] This outline covers the subject completely from a bacteriologic point of view, and I can do no better than to submit

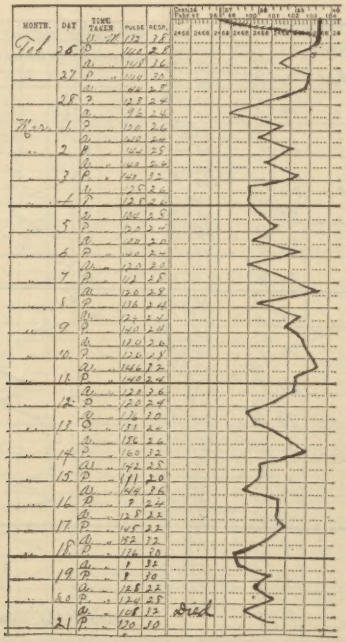

FIG. 4.

my description of this microorganism in the form advised by this committee. It may be well to speak of the extreme difficulty of cultivating the diplococcus intracellularis upon the ordinary culture-media—a fact already pointed out by Councilman.[11] The microorganism seems to thrive best on Löffler's blood-serum and it was upon this medium that my inoculations were first made; later, the other media were

inoculated and thus the microorganism was studied thoroughly. Had I immediately inoculated or plated the microorganism upon agar, it is doubtful whether a growth would have been obtained. Photographs of the colonies were taken—a procedure especially recommended by the committee. The diplococcus intracellularis is considered by some to be allied to the gonococccus since the method of division, the cultural behavior and the fact that it is found within the pus-cell are identical characteristics of both micoorganisms. Ghon, of Vienna, has given a description of this microorganism and claims that it corresponds in cultural behavior to the gonococcus of Neisser. Ghon and Jaeger found the meningococcus in the nasal secretions in many of these cases, and I have been able to do so in many instances. No record is found in Ghon's cases of a demonstration of the microorganism in the purulent discharge from the ear. In nearly all the cases which were complicated by purulent discharge from the ear, I was able to recover the diplococcus intracellularis.

My experience has been that the Gram method of staining as a differential test between the diplococcus intracellularis and the micrococcus lanceolatus has but little value. In many of my cases I found that the diplococcus intracellularis would be decolorized, according to Gram, and in other cases it would retain its color: again, in some cases, the diplococcus intracellularis would be stained, according to Gram, after being grown for but a short time, and when successive transfers had been made, and the microorganism had passed through the cycle of cultural life for a week or two, it would show a decolorization when subjected to the Gram method of staining. In the same cover slip preparation, some diplococci would be deeply stained, and others very feebly.

The complete description of the microorganism now follows:

I.—MORPHOLOGY.

Source.—1. Cerebrospinal fluid, obtained from man by (*a*) lumbar puncture, (*b*) postmortem specimens.
2. Brain and spinal cord tissue.

3. Cerebrospinal fluid, pus, cerebral and cord tissue of animals used for experimental inoculations, viz., dogs, cats, and a rabbit.

4. Secretions from the nose and ear.

5. Pulmonary tissue of man and animals dead of secondary pneumonia.

Habitat.—Cerebrospinal fluid; intrameningeal spaces, nose, and ear.

Morphologic examination of agar-culture, grown 28 hours, at 18°–20° C.; ditto, grown 28 hours, at 36°–38° C.; ditto, grown for 48 hours, at 36°–38° C.; ditto, grown for 60 hours, at 36°–38° C.

Morphologic examination of Löffler's blood-serum culture (as above).

Morphologic examination of gelatin culture (as above).

Morphologic examination of broth (as above).

Morphologic examination of glycerin-agar (as above).

Morphologic examination of potato (as above).

Morphologic examination of milk (as above).

Morphologic examination of litmus milk (as above).

Diplococcus; tetracoccus in a few cases; in few cases, chains of not more than six.

Size.—About size of gonococcus. Great variation in size was noted: as seen in the pus-cell, the diplococci were about the size of the gonococci; when separated in pure culture, they became a little larger, and they increased in size in proportion to the number of transfers that were made, *i. e.*, at the end of 2 weeks, if transfers were made daily, the size of the microorganism far exceeded its original size. They also varied in size with the character of the culture upon which they were grown; they attained the largest size upon agar, and retained their size most uniformly upon Löffler's blood-serum.

It stains with the standard watery dyes easily, especially with fuchsin. It is decolorized by Gram's method in some cases, and retains its color in others, as above stated.

No capsule observed.

No spore-formation.

No vacuoles observed.

		Age	Sex	Family History	Occupation	Sanitary Condition	Chill	Sign of Kernig	Difficulty of Deglutition	Projectile Vomiting	Diarrhœa	Herpes Labialis	Eruption	Tache Cerebrale	Headache	Hyperæsthesia	Retraction of Head	Pain along Spine	Delirium	Coma	Paralysis	Tremors	Knee Jerk	Pneumonia	Pulse	Albumins	Sugar	Diaz	Insensibility of Pupil	Nystagmus	Strabismus	Retracted Abdomen	Opisthotonos	Result?	Duration of Disease	Orthotonos	Perlorphobia	Convulsion	Joint Affection
Case	I	33 yrs	Male	Negro	Labor	Poor	None	Yes	Yes	No	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	None	Yes	Exaggerated	Yes	Rapid	None	None	Yes	Yes	No	Yes	Yes	Died	13 days	No	Yes	No	No
"	II	9 days	Female	Good	Nihil	Poor	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes(?)	Yes	Yes	Yes	Yes	No	Ocular	Yes	Normal	No	Rapid	None	None	No	Yes	Yes	Yes	Yes (Left)	Yes	Yes	Died	2 days	No	"	No
"	III	16 yrs	Male	Neg	Labor	Poor	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	None	Yes	Exaggerated	No	Rapid	Yes	None	Yes	Yes	No	No	No	Yes	Yes	Died	21 "	Yes	"	"
"	IV	22 yrs	Female	Good	Domestic	Good	None	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Ocular	Yes	"	No	Rapid	Yes	None	No	Yes	No	Yes	No	Yes	Yes	Recovered	17 "	No	"	"
"	V	38 yrs	Male	Neg	Neg	Neg	?	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Ocular Ptosis	Yes	"	No	Rapid	Yes	None	Yes	Yes	No	Yes	No	Yes	Yes	Died	4 " 0	No	"	"
"	VI	21 yrs	Male	Good	Labor	Poor	Yes	Yes	No	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	No	None	Yes	Normal	No	Rapid	Yes	None	Yes	No	Yes	No	No	Yes	Yes	Died	35 "	Yes	"	"	"
"	VII	26 yrs	Male	Neg	Labor	Poor	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	No	None	Yes	Exaggerated	No	Slow	Yes	None	Yes	Yes	No	No	No	Yes	No	Recovered	26 "	No	"	"	"
"	VIII	9 mos	Female	Neg	Nihil	Poor	Yes	Yes	Yes	Yes	No	Yes	No	Yes	No	Yes	Yes	No	No	None	Yes	Normal	No	Rapid	Yes	None	No	Yes	No	No	Yes (Left)	No	Yes	Died	20 "	Yes	Yes	"	"
"	IX	8 yrs	Female	Neg	Nihil	Poor	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Ocular	Yes	Exaggerated	No	Rapid	Yes	None	No	Yes	Yes	No	Yes (Left)	Yes	No	Died	22 "	Yes	Yes	"	No
"	X	5 yrs	Female	Good	Nihil	Poor	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	External Rectus	Yes	"	No	Rapid	Yes	None	No	Yes	Yes	Yes	No	Yes	Yes	Died	37 "	Yes	Yes	No	No
"	XI	3 yrs	Male	Good	Nihil	Poor	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	None	No	"	Yes	Rapid	No	None	No	Yes	No	No	Paresis Yes	Yes	Yes	Died	22 "	Yes	Yes	No	"
"	XII	3 1/2 yrs	Female	Good	Nihil	Poor	No	Yes	Yes	No	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	None	No	Normal	No	"	Yes	Yes	Yes	Yes	No	No	(Left) Yes	No	Yes	Died	4 "	No	Yes	"	"
"	XIII	23 yrs	Male	Good	Labor	Poor	Yes	Yes	Yes	Yes	No	No	No	?	Yes	No	Yes	Yes	Yes	No	None	Yes	Absent	No	"	No	No	No	Yes	No	No	No	Yes	Yes	Recovered	23 "	No	"	"	"
"	XIV	3 yrs	Male	Good	Nihil	Poor	Yes	Yes	Yes	No	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Auditory	No	Exaggerated	No	"	No	No	No	Yes	No	No	No	No	Yes	Recovered	10 "	No	"	"	"
"	XV	22 yrs	Male	Good	Labor	Poor	No	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Ptosis Ocular	Yes	Absent	No	Slow	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Died	2 "	No	"	"	"
"	XVI	53 yrs	Femal	Neg	Neg	Fair	No	Yes	Yes	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	None	No	Absent	No	Rapid	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	Died	7 "	Yes	Yes	"	No
"	XVII	35 yrs	Male	Neg	Carpt	Poor	No (?)	Yes	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	No	None	Yes	Absent	No	Very Rapid	Yes	No	Yes	Yes	No	No	No	Yes	Yes	Died	13 "	Yes	No	"	"
"	XVIII	18 yrs	Male	Neg	Farm	Poor	Neg	Yes	Yes	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Internal Rect. us	Yes	Absent	No	Rapid	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Died	16 "	No	Yes	"	"
"	XIX	26 yrs	Male	Neg	Lab.	Poor	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Ptosis	Yes	Exaggerated	No	"	Yes	No	Yes	No	Yes	No	No	Yes	Yes	Died	2 "	No	Yes	"	Yes
"	XX	7 yrs	Female	Neg	Nihil	Poor	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes (?)	Yes	Yes	Yes	Yes	Yes	None	No	Normal	No	"	No	No	No	Yes	Yes	No	No	Yes	Yes	Recovered	12 "	Yes	"	"	No
"	XXI	45 yrs	Female	Good	Nihil	Poor	Neg	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	None	Yes	Normal	No	"	Yes	No	No	Yes	No	No	No	Yes	Yes	"	26 "	No	"	"	No
"	XXII	25 yrs	Male	Neg	Labor	Poor	Neg	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	None	Yes	Absent	No	"	Yes	No	No	Yes	No	No	No	No	Yes	Died	4 "	No	"	"	No
"	XXIII	9 yrs	Male	Neg	Nihil	Poor	Neg	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	None	Yes	"	No	Rapid	No	No	No	Yes	No	No	No	No	No	Died	3 "	Yes	"	"	No
"	XXIV	17 yrs	Female	Good	Nihil	Fair	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	None	Yes	Exaggerated	No	"	No	No	No	Yes	No	No	No	No	Yes	Recovered	14 "	No	"	"	"
"	XXV	16 yrs	Female	Good	Servt	Poor	No	Yes	Yes	No	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	None	Yes	"	Yes	"	Yes	No	No	No	No	No	No	Yes	No	"	17 "	Yes	Yes	"	"
"	XXVI	8 yrs	Male	Good	Nihil	Poor	No	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	None	Yes	"	No	"	No	No	No	Yes	Yes	Yes	No	No	Yes	"	21 "	No	Yes	No	"
"	XXVII	6 yrs	Female	Good	Nihil	Fair	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	None	Yes	"	No	"	No	No	Yes	Yes	Yes	No	No	Yes	Yes	Died	6 "	No	"	No	No
"	XXVIII	28 yrs	Male	Good	Painter	Fair	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	None	No	"	No	Rapid	Yes	No	Yes	Yes	No	No	No	No	Yes	Died	7 "	Yes	"	No	No
"	XXIX	26 yrs	Male	Good	Farm	Poor	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	None	Yes	"	No	Rapid	Yes	No	Yes	Yes	No	No	No	No	Yes	Recovered	13 "	Yes	"	"	No
"	XXX	12 yrs	Female	Good	Nihil	Poor	No	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	None	Yes	Absent	No	"	No	No	No	Yes	No	No	No	No	Yes	Recovered	16 "	No	Yes	Yes	No
"	XXXI	21 yrs	Male	Good	Dentist	Good	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	None	Yes	"	No	"	"	No	Yes	Yes	Yes	No	No	No	Yes	Died	15 "	Yes	No	No	Yes
"	XXXII	31 yrs	Male	Good	Labor	Poor	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No.	None	Yes	"	No	"	No	No	No	Yes	No	No	No	No	Yes	Recovered	10 "	No	Yes	No	No
"	XXXIII	21 yrs	Female	Good	Servt	Poor	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Ocular	Yes	Exaggerated	No	Rapid		No	Yes	Yes	Yes	Yes	No	Yes	Yes	Died	7 "	No	Yes	No	No
"	XXXIV	39 yrs	Male	Neg	Labor	Poor	Neg	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	"	No	Rapid	No	No	No	Yes	Yes	No	No	Yes	Yes	Died	4 "	Yes	Yes	No	No

FIG. 6.—Cerebrospial meningitis—Compilation of cases.

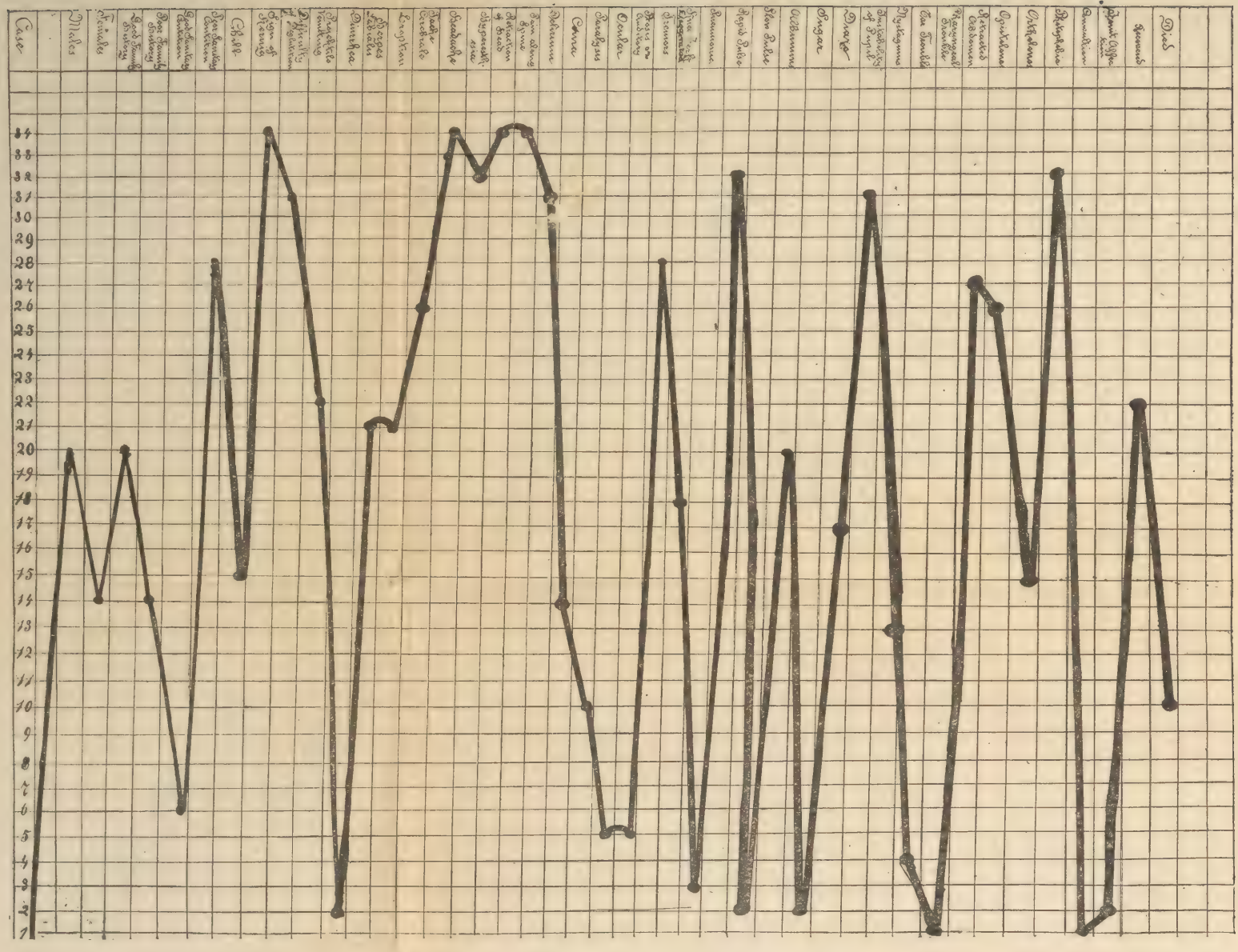

FIG. 7.—Graphic representation of epidemic of cerebrospinal meningitis.

No crystals observed.
Non-motile.
Pleomorphism, as above noted.
Growth, at 18°–20° C., is less abundant than that at 36°–38° C.
Thermal death-point, 55° C.; time of exposure, 10 minutes; permanence of morphologic characters . . yes.
Optimum temperature, 38° C.; growth limited; maximum, 50° C.; minimum, 18° C.
Optimum reaction of media, from 3.5% more than neutral.

II.—BIOLOGY.

Gelatin Plate.

(*Neutral.*)

Deep Colonies.	Surface Colonies.
Size, 2 to 3 mm.	Size, 3 to 4 mm.
Rather circular.	Round.
Margin, dark.	Margin, lighter than center.
Texture, homogenous.	Texture, granular and wavy.
Faint growth under mica plate.	

Agar Plate.

(*Neutral.*)

Deep Colonies.	Surface Colonies.
Little larger than gelatin.	Same as gelatin.
Round.	Round.
Dark margin.	Light margin.
Granular.	More coarsely granular.
White.	White.

Gelatin Tube.

(*Neutral.*)

Puncture:—

One inch and a half in length.
Straight, linear puncture.
Faint line, white color.
Faint growth along stroke.
More abundant growth on surface.

Streak :—

Flat, straight, tapering towards the top.
Thicker in middle, margin less dense.
Does not stand up above the surface to any extent.
Transmits light moderately.
Dull, reflecting light poorly.
White in color.
Lustre is dull.

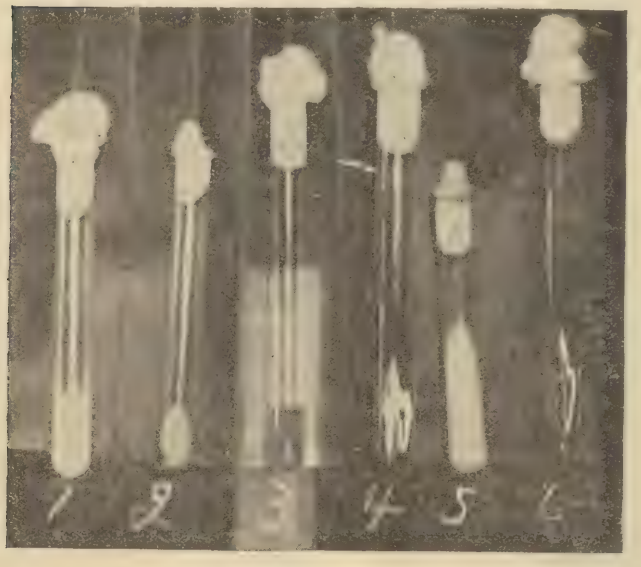

FIG. 5.—Cultures of the Diplococcus Intracellularis Meningitidis:

1. Milk, showing coagulation.
2. Potato, 30 hours old.
3. Bouillon, 24 hours old.
4. Glycerin-agar, 30 hours old.
5. Löffler's blood-serum, 24 hours old.
6. Plain agar, 24 hours old.

Change in medium :—

No change in consistence, color, or odor.

AGAR TUBE.

Neutral.

Streak :—

Two and a half inches.
Grows in a wavy line, about 2.5 mm. wide.

Growth at first is limited to the appearance of a few small white points along the streak; these points grow larger after 18 hours, and, as they increase in size, more small points appear, and, at the end of 28 hours, they have coalesced, and formed one continuous white streak. The streak shows the primary construction of points for 30 hours by minute protuberances which project above the surface; but after that time the surface becomes level.

Surface relief accordingly is well marked.

Light is transmitted for 20 hours, but not thereafter.

Light is reflected from the individual colonies before coalescence, but not after the formation of the streak.

White in color.

Luster is dull.

Change in medium:—

No change in color, consistence, or odor.

Nutrient Bouillon in Test-Tube.

It becomes turbid at 38° C., after 18 hours. Clears on standing. On shaking, masses are seen to arise from the bottom of the tube. No change in the color of broth noted; no formation of pellicle.

Milk.

No visible change in 24 hours at 38° C. Does not curdle in 48 hours at 18°–20° C.; curdles in 48 hours at 36°–38° C.; curdles on boiling. In litmus-milk, the red color, showing acid reaction, is developed, after 24 hours at 18°–20° C., and in 12 hours at 36°–38° C. No odor is developed. The curd forms in small fragments.

Glucose Bouillon in Fermentation-Tube.

In the bulb, the fluid becomes turbid, and a fine, flocculent mass forms in the connecting tube, while the fluid in the closed tube remains clear at the extreme top, but is slightly turbid in the lower part.

This clears on standing for 6 hours. No color develops.

Potato.

Growth occurs in the form of a shining, yellowish-white, viscid, smeary substance, after 18 hours at 36° to 38° C.

Löffler's Blood-Serum.

After from 15 to 18 hours, minute white colonies appear, separated from each other by a distinct interval. These colonies increase in size and others at the same time appear, so that at the end of 24 or 26 hours, a white streak covers the surface. It still shows its primary construction in that the white, separated colonies stand up above the surface. A further change noted at the expiration of 30 hours is the change in color from an almost pure white to a dull, brownish-white color. At the end of 48 hours the growth is dead so far as further growth in other tubes which are inoculated is concerned.

No pigment is developed in the medium.

The microorganism dies within two days if it is not transferred to a fresh tube. One tube of the microorganisms can remain virulent for 70 days, according to Ghon ;[12] in order to do this, the cultures should not be allowed to dry out, and they should be kept at a temperature not below 25° C.

It is an aerobic, facultative anaerobic microorganism. It is said to be pathogenic for dogs, cats, rabbits and guineapigs. My inoculations upon animals were limited to dogs, cats, and one rabbit. The results of these experiments are highly interesting, as an attempt was made to show a correspondence between the virulence of the microorganism in a particular case in man with the virulence of the fluid or culture from that case when injected into the lower animals. In nearly every case this was demonstrated conclusively. Six dogs, 12 cats and 1 rabbit were inoculated. In the first two experiments upon dogs, trephination was resorted to as a means of introducing the microorganisms into the cranial cavity ; this was afterwards modified by the use of a long exploratory needle and syringe by which the animals could be

quickly and just as surely inoculated with the diplococcus intracellularis. It is also a curious fact that the dogs manifested symptoms more closely approaching the disease as it is seen in man than did the cats. The first dog was inoculated with material from a man who had succumbed to the disease in 24 hours after the onset; this dog died in convulsions 6 hours after coming out of the anesthetic. The second dog was inoculated with material from a man who had succumbed to the malady 2 weeks after the initial symptoms, and this dog lived 10 days, finally dying in convulsions. This second dog began to show symptoms on the second day following the inoculation, lying on its back, with rigidity of the spine, and would not partake of food for 3 or 4 days. It began to have convulsions on the tenth day and died in opisthotonos. The temperature of this dog was taken before the inoculation, and it was 100° F. It had an average temperature of 104° to 107° F. until its death. The third dog was inoculated with cultures obtained from the second dog postmortem, and it died in about 2 weeks, displaying about the same conditions as the second dog. A fourth dog was inoculated with a pure culture of the diplococcus intracellularis taken postmortem from a pregnant woman who had lived but 2 days after the acute onset of the disease, and this dog lived 4 days, finally dying in convulsions. The fifth dog was inoculated with a pure culture obtained from the fetus of the above woman, and this dog died 2 days thereafter, in convulsions, as did another dog which was inoculated from cultures from the mother's ear. The dogs all manifested symptoms referable to the disease in some way or another: they had convulsions, had a febrile temperature and showed that they were acutely ill.

The results of the inoculations upon cats were equally gratifying in so far as a correspondence between the virulence of the infection in the patient and the virulence of the material from that case when inoculated into the cats was concerned. The cats did not, however, show evidences of the disease in the way of symptoms as did the dogs. Three of the cats had convulsions antemortem, but the other 9 did

not have them. One cat had marked opisthotonos while the others did not. One cat was inoculated with cultures obtained from a patient who subsequently recovered after being sick 6 weeks; the cultures were taken at the end of the third week of the disease. This cat apparently recovered after being confined for about one month; the cat was killed with chloroform, and at the autopsy some thickening of the meninges was found but no exudate. Cultures taken from the meninges were barren of growth. This was the only cat that was not killed by the disease. It may be well to add here that postmortem examinations were made upon all the animals, and cultures were thus obtained. The pathologic conditions found in these animals corresponded closely to those found in man, of which mention will be made later on. In order to demonstrate the fact that the diplococcus intracellularis is the essential cause of the secondary pneumonia which is sometimes found in connection with epidemic cases of cerebrospinal meningitis, I injected pure cultures of the microorganism into the pleural cavities of two cats: they died after 2 days and at the postmortem examination typical croupous pneumonia was found. The diplococcus intracellularis was recovered in pure culture from these pneumonic lungs. No signs of meningitis were found at autopsy in these two cats. The rabbit which was inoculated died after 2 days, being killed with cultures from a patient who had lived but 2 weeks after primary infection. Thus the pathogenesis of the diplococcus intracellularis was clearly proved.

Of the 34 cases seen by me, 22 were fatal and 12 resulted in recovery—a mortality of 64 $\frac{2}{3}$%. Autopsy was held in 21 of the fatal cases, the body of the twenty-second man having been removed by his family before we had time to conduct a postmortem examination. The findings in these cases were nearly parallel both as regards microscopic and macroscopic results. It is for this reason that the pathology of the affection is discussed *in toto*. In this place it is incumbent upon me to speak of the great value of lumbar puncture as a diagnostic measure in cases of supposed epidemic cerebrospinal meningitis. It is an

absolutely harmless procedure and in some cases in which there is an abundant exudation of a serous nature improvement seems to follow its performance; this was noticed in one case by me. Lumbar puncture offers the only means of a differential diagnosis between a sporadic and an epidemic case of cerebrospinal meningitis. In the cases reported, lumbar puncture was performed in every instance save one, and in the fatal cases the microorganism was also separated from the tissues. As stated above, the micrococcus lanceolatus was demonstrated in the cerebrospinal fluid and in the tissues postmortem of but one case. The puncture should be made on a level with the crest of the ilium and the aspirating needle should be directed slightly upward and inward, the point of the needle puncturing the skin about one half inch from the spinous processes to either side. By feeling the way in, the needle readily enters the spinal cavity. If the fluid does not flow rapidly, the patient should be elevated in bed by raising the shoulders. It is recommended not to resort to the use of the aspirating syringe.

The postmortem findings in these cases were uniform and will be discussed accordingly. The gross pathologic lesions consisted, in the acute cases, of a great injection of the vessels of the pia arachnoid with a purulent exudation over the meningeal surfaces. In some cases this exudation of pus was confined exclusively to the base of the cerebrum, but in other cases it could be made out over the entire surface of the meninges. In all the cases the same purulent exudate was found spread over the pia arachnoid of the cord. In the very acute cases—cases which survived but a day or two after the onset—hyperemia of the pia arachnoid alone was present or predominated over the purulent exudation. The cerebral tissue was softer and more friable than it is in other conditions. Upon opening the ventricles by the usual "postmortem incisions" they were found to contain a purulent fluid in greater or less amounts in different cases. In some cases there was only a smeary coat of pus lining the ventricles, while in other cases the purulent exudation into the ventri-

cles was so great that it amounted almost to a hydrocephalus internus. When the purulent exudation was confined mainly to the base of the cerebrum, there were strong adhesions between the cerebrum and the cerebellum due to the organization of this purulent mass. Sections of the meninges, the cerebral and cord tissues, cranial and spinal nerves were hardened in Zenker's fluid and alcohol and imbedded in celluloidin. The intracellular diplococci were demonstrated in these sections by staining with eosin followed by Unna's methylene-blue. "The advantage of Unna's methylene-blue, which is more alkaline than Löffler's, is that it stains bacteria and nuclei in tissues hardened in Zenker's fluid, which gives a more pefect fixation of the tissue-elements than either alcohol or sublimate."[13] The meninges showed mainly purulent infiltration. The most marked pathologic change in the gray matter was the increase in size in the neuroglia-cells with an increase in the nuclei of the protoplasm.

In sections of the cord, stained by Nissl's method, the two changes already pointed out by Barker were noted:[14] a disintegration in the stained section of the individual Nissl bodies, especially in those of the dendrites and of the periphery of the cell-body; secondly, a breaking down in the center of the cell and a displacement of the nucleus to the periphery of the cell. These two changes are due, first to the direct action of the bacteria upon the tissue in contiguity to the meninges of the cord; secondly, to the fact that axones of these cells are injured on the surface of the cord and consequently the second change takes place, *i. e.*, a breaking down in the center and a displacement of the nucleus to the periphery of the cell. This second effect is nothing more or less than the "reaction at a distance of Marinesco." This secondary effect, as seen particularly in the nucleus of Clark's column, is due to the fact that axones derived from that nucleus and running in the direct cerebellar tract are superficially placed in the medulla, where the purulent exudation is ofttimes greatest in these cases. The cranial nerves showed various degrees of degeneration and inflammation, particularly

the second and eighth. In some cases pus was found within the eyeball, coincidently with the existence of a choroiditis. It is an open question whether pus follows the course of the optic nerve into the eye or whether it is formed within the eye as a kind of metastatic process of meningitis. It has been said by Dr. John Green, of St. Louis, that he has known of cases of this disease in which the pus seemed to form within the eye—sometimes to a great extent and even so much as to completely fill the eye, pushing out the vitreous and perforating the cornea. In view of this fact we may say that the existence of pus within the eye is a complication and not part of the meningeal trouble. The auditory nerve showed distinct degeneration, as did some of the spinal nerves. Examination of the other organs revealed the impress of the toxic condition, *i. e.*, acute hemorrhagic nephritis, septic spleen in some cases, myocarditis, pneumonia and a gangrene of the lung in one instance.

These 34 cases of epidemic cerebrospinal meningitis when considered as a whole give us a beautiful picture of the symptomatology of this affection. In this group of cases, every symptom which has been described as belonging to this disease was found, and indeed some of the individual cases displayed a clinical aspect in perfect accord with the type of the affection. It is for this reason that I prefer to discuss the symptomatology of the epidemic as a whole and not seriatim. Not only will words be saved by this method, but it is hoped that the clinician will be more fully impressed with the symptoms found. I have prepared a chart of these cases with a list of symptoms as recorded by the health-department of the city of St. Louis in their recent investigation of the recent St. Louis epidemic. A graphic representation of these cases is also appended. I will briefly narrate these symptoms, with ages of the patients and duration of the disease. The oldest patient was a woman of 53 years; the youngest, a child of 9 days. A majority of the cases occurred among adults over 16 years of age. There were 20 males and 14 females. In some of the cases it was impossible to obtain a

complete family and personal history, as they came to the hospital unaccompanied. The sanitary conditions to which these patients were subjected before their illness were in all but 2 cases definitely known to have been very bad. In the majority of cases it was found that squalor and filth could be impartially said to have played a part in the infection of the patient with meningitis. In 15 cases the onset of the disease was marked by a chill. In every case the sign of Kernig was present, thus adding another confirmation to the statement of Herrick,[15] "that the sign of Kernig is as pathognomonic of meningitis as the rose-spots of typhoid fever or the murmurs are of endocarditis." As early as 1882, Kernig, of St. Petersburg, called attention to this sign, which he thought was found only in affections of the pia mater and which was never lacking in inflammations of that membrane. This was subsequently confirmed by Henoch, Bull, Blüm and Friis. Netter[16] later confirmed these observations and cited cases. The sign of Kernig is elicited in the following way: the patient is placed in dorsal decubitus, care being taken that the legs are relaxed and fully extended at the knees. When the patient is raised in bed by the shoulders, it is found that the knees are more or less flexed, and, despite all efforts, cannot be extended on account of contracture of the posterior muscles of the thighs. Complete extension becomes possible when the patient is placed upon the back again. It is dependent upon a marked flexor contracture. Netter[15] found this sign present in 41 instances among 46 cases of meningitis of different kinds, or about 90%. Herrick has recently made observations upon this sign in 19 cases with 6 autopsies.[17] It was present in 17 of these cases, and in 2 in which it was not found but a single examination was made only a short time before death when there was a general laxity of all the muscles. It was, therefore, of considerable value in some of the cases as a means of diagnosis. Netter[15] believes that the presence of this sign confirms the diagnosis of meningitis when the symptoms are obscure and suggests a latent meningitis when it is the only symptom present. In 25 healthy patients

examined by Herrick this sign was not present. In 100 cases of patients sick with other diseases, it was present but twice and absent in 98 cases.

Difficulty of deglutition was present in 31 cases; projectile vomiting was present in 22 cases. Diarrhea was noted but twice; joint-affections were present in only 2 cases. Herpes labialis was present in 21 cases; an eruption, either petechial or maculopapular, was present in 21 cases. Orthotonos was present in 15 cases, and opisthotonos in 26 cases. Tâche cerebrale was noted in 26 instances. Headache, retraction of the head, and pain along the spine were constantly present. Delirium was present in every case save 3. Coma was present in 14 instances. Paralysis was a symptom found in 10 cases, and included ptosis, strabismus, and auditory involvement. Tremors, particularly of the lingual and facial muscles, were noted in 28 cases. The patellar reflex was exaggerated in 18 cases, normal in 6, and absent in 10 cases. Croupous pneumonia was made out in 3 instances. The pulse was rapid in all the cases except 2; one of the patients, with a slow pulse, died, after being sick 2 days, while the other recovered, after an illness of 20 days. The urine showed the following reactions: albumins in 20 cases; sugar present in 2 cases; diazo-reaction positive in 17 cases, and absent in 17. Casts, epithelial and granular, were found in 3 cases. Instability of the pupil was made out in 31 cases. Nystagmus was present in 13 cases. Otitis media purulenta was present in 4 cases. Pharyngeal trouble was noted once. Retraction of the abdomen was noted in 27 cases, and absent in 7. The duration of the disease varied from 2 to 37 days, an average duration of $14\frac{3}{16}$ days. In Case III, there was a history of an attack of convulsions on the day before entrance into the hospital. In Case XIII, there was a statement from the patient's father, saying that his son (patient) had been struck on the back of the neck with an iron wheel on the day before taken acutely ill; he did not, however, manifest any symptoms of concussion at the time of the receipt of the injury. Case XX had a well-marked bulging of the fontanelle. We have in Cases VIII and IX the only probable instance of

contagion in all the cases. Case VIII was taken ill on one day, and, on the following day, its playmate, Case IX, was similarly affected. Of course, both might have been infected from the same source, and not one from the other. In no case was I able to trace any conveyance of the disease from one patient to another. We must take into consideration the extreme difficulty of following the movement of patients in a large city like St. Louis. Among these 34 cases of epidemic cerebrospinal meningitis, there was one of transmission of the disease in utero, as demonstrated by pathologic and bacteriologic findings. I will make this the subject of another paper, and will present it before this Association if it be desired.

In conclusion it can be said of this disease in general and of its manifestations in these cases in particular, that—

1. It is a specific infectious disease.

2. It is not highly contagious, but only contagious in the sense that tuberculosis pulmonalis is contagious.[19]

3. The diplococcus intracellularis meningitidis is the prime etiologic factor in the causation of epidemic cerebrospinal meningitis.

4. In all suspected cases of meningitis, lumbar puncture should be resorted to as a means of differential diagnosis between an epidemic and a sporadic case.

5. The Gram method of staining is a rather uncertain means of differentiating the diplococcus intracellularis from the micrococcus lanceolatus.

6. The diplococcus intracellularis is especially pathogenic for dogs and cats.

7. The virulence of the infection, *i. e.*, of the diplococcus intracellularis, varies in different cases and in different periods of its visitation upon the same patient; that the virulence of the infection tends towards an attenuation with the further progress of the disease and that in the more chronic cases which have gone beyond the period of one month, the virulence of the infection is almost lost.

8. The sign of Kernig is pathognomonic of meningitis.

9. Epidemic cerebrospinal meningitis can be transmitted in utero.

BIBLIOGRAPHY.

[1] Barker and Flexner: *Amer. Jour. Med. Sci.*, 1894.
[2] Jaeger: *Zeitschrift f. Hyg. u. Inf. Krankheiten*, Leipzig, 1895.
[3] Councilman, Mallory and Wright: *Amer. Jour. Med. Sci.*, March, 1898.
[4] Class: *The Journal of the Amer. Med. Asso.*, March 25, April 1, April 8, 1899.
[5] Vieussieu: *Hufeland's Journal*, Heft 2, 1805.
[6] Weichselbaum: *Fortschritte d. Med.*, 1887.
[7] Jaeger: *Loc. cit.*
[8] Barker and Flexner: *Johns Hopkins Hospital Bulletin*, February, 1898.
[9] Class: *Loc. cit.*
[10] Report of Committee of American Bacteriologists to the Committee on the Pollution of Water Supplies of the American Public Health Association, submitted at the meeting of the Association at Philadelphia, September, 1897.
[11] Councilman: *Amer. Jour. Med. Sci.*, March, 1898. *Johns Hopkins Hospital Bulletin*, February, 1895.
[12] Ghon: See reference 4.
[13] Councilman: *Amer. Jour. Med. Sci.*, March, 1898.
[14] Barker: *Loc. cit.*
[15] Herrick: *Medical News*, May 13, 1899.
[16] Netter: *Soc. médicale des Hôpitaux*, July 22, 1898.
[17] Herrick: *Loc. cit.*
[18] Netter: *Loc. cit.*
[19] Class: *Loc. cit.*